

ABSTRACT OF THE DISCLOSURE

The present invention describes a method for identifying bases in an RNA sequence that are relatively inaccessible to solvent as the result of intramolecular and/or intermolecular interactions. Embodiments of the invention can be used to evaluate the three-dimensional structure of an RNA molecule or the interactions between an RNA molecule and a molecule capable of binding to RNA, such as another nucleic acid or an RNA-binding protein. The invention involves contacting an RNA molecule with a cleavage reagent capable of partially hydrolyzing said RNA molecule, wherein said partial hydrolysis is attenuated in a region of said RNA molecule that is relatively inaccessible to solvent; and separating and detecting the cleaved RNA by IP-RP-HPLC, wherein the absence of cleavage events in a region of the RNA indicates that said region is relatively inaccessible to solvent. The separation medium is preferably substantially free of multivalent cations capable of interfering with polynucleotide separations.